L Number	Hits	Search Text	DB	Time stamp
-	218	(gene ADJ silencin$5) and (animal$5 or mammal$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:33
-	182	((gene ADJ silencin$5) and (animal$5 or mammal$5)) and repeat$10	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/08 12:53
-	174	(((gene ADJ silencin$5) and (animal$5 or mammal$5)) and repeat$10) and promoter	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/08 12:59
-	32	((((gene ADJ silencin$5) and (animal$5 or mammal$5)) and repeat$10) and promoter) and tandem	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/08 12:56
-	34	(gene ADJ silencin$5) SAME (animal$2 or mammal$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/08 13:03
-	10	(gene ADJ silencin$5).clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/09/08 13:03
-	369	gene ADJ silencin$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 11:44
-	2744	DOUBLE ADJ STRANDED ADJ RNA	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:38
-	2034	(DOUBLE ADJ STRANDED ADJ RNA) and (inhibition or silen$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 11:59
-	1858	((DOUBLE ADJ STRANDED ADJ RNA) and (inhibition or silen$5)) and (animal or mammal)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 11:59
-	1803	(((DOUBLE ADJ STRANDED ADJ RNA) and (inhibition or silen$5)) and (animal or mammal)) and gene	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 12:00
-	1847	(((DOUBLE ADJ STRANDED ADJ RNA) and (inhibition or silen$5)) and (animal or mammal)) and gene$5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 12:01
-	1587	((((DOUBLE ADJ STRANDED ADJ RNA) and (inhibition or silen$5)) and (animal or mammal)) and gene$5) and (antisense or sense)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 12:01
-	4	(((((DOUBLE ADJ STRANDED ADJ RNA) and (inhibition or silen$5)) and (animal or mammal)) and gene$5) and (antisense or sense)) and silen$5.clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/10/31 12:02
-	0	WO ADJ "941550"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:34
-	6	WO ADJ "9401550"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:36
-	121	AGRAWAL-Sudhir.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:37

-	119	AGRAWAL-Sudhir.in. and oligonucleotide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:38
-	75	(AGRAWAL-Sudhir.in. and oligonucleotide) and (sense or antisense)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:41
-	12	((AGRAWAL-Sudhir.in. and oligonucleotide) and (sense or antisense)) and loop	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:46
-	1	435/325.ccls. and AGRAWAL-Sudhir.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:49
-	2	435/320.1.ccls. and AGRAWAL-Sudhir.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:49
-	75	AGRAWAL-Sudhir.in. and (sense or antisense)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:50
-	10	AGRAWAL-Sudhir.in. and (sense or antisense).clm.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:50
-	9	AGRAWAL-Sudhir.in. and (SELF-STABILIZED ADJ OLIGONUCLEOTIDES)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/07 11:56

(FILE 'HOME' ENTERED AT 10:45:14 ON 12 NOV 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS, MEDICONF' ENTERED AT 10:45:23 ON 12 NOV 2002

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L1        40392 S GENE (L) SILEN?
L2         3154 S L1 AND (TANDEM OR REPEAT)
L3           75 S L2 AND (SENSE OR ANTISENSSE)
L4           29 DUP REM L3 (46 DUPLICATES REMOVED)
L5           29 FOCUS L4 1-
L6          457 S D HIS
L7            9 S L5 AND PY<=1998
L8            0 S L4 AND GRAHAM?/AU
                E GRAHAM MICHAEL?/AU
L9           20 S E1
L10           5 S E2
L11          25 S L9 OR L10
L12          18 DUP REM L11 (7 DUPLICATES REMOVED)
L13           0 S L12 AND L4
L14           0 S L12 AND L2
L15           3 S L12 AND L1
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=> d an ti so au ab pi l15 1-3

L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:713532 CAPLUS
DN 135:268121
TI Post-transcriptional **gene silencing** via reduction of a target transcript translation for manipulation in the phenotype of an animal
SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2
IN **Graham, Michael Wayne**; Rice, Robert Norman; Murphy, Kathleen Margaret; Reed, Kenneth Clifford
AB The present invention relates generally to a method of inducing, promoting or otherwise facilitating a change in the phenotype of an animal cell or group of animal cells including a animal comprising said cells. The modulation of phenotypic expression is conveniently accomplished via genotypic manipulation through such means as reducing translation of a target transcript (co-suppression). One aspect of the present invention provides a genetic construct comprising a nucleotide sequence substantially identical to a target endogenous **gene** of a vertebrate animal cell, and further comprises a nucleotide sequence complementary to said target **gene**, wherein the sequences identical and complementary to said target **gene** are sepd. by an intron sequence. In prefered embodiment said intron sequence is an intron from a **gene** encoding .beta.-globin, and even more preferred the .beta.-globin intron is human .beta.-globin intron 2. The ability to induce, promote or otherwise facilitate the **silencing** of expressible genetic sequences provides a means for modulating the phenotype in, for example, the medical or veterinary industries. Expressible genetic sequences contemplated by the present invention including not only **genes** normally resident in a particular animal cell (i.e. indigenous **genes**) but also **genes** introduced through recombinant means or through infection by pathogenic agents such as viruses.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001070949	A1	20010927	WO 2001-AU297	20010316

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 2001:558239 CAPLUS

TI Suppression of **gene silencing**: a threat to virus-resistant transgenic plants
SO Trends Plant Sci. (2001), 6(5), 246-247
CODEN: TPSCF9; ISSN: 1360-1385
AU Mitter, Neena; Sulistyowati, Emy; **Graham, Michael W.**; Dietzgen, Ralf G.
AB Unavailable

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
AN 1998:745287 CAPLUS
DN 130:63748
TI Virus resistance and **gene silencing** in plants can be induced by simultaneous expression of sense and antisense RNA
SO Proceedings of the National Academy of Sciences of the United States of America (1998), 95(23), 13959-13964
CODEN: PNASA6; ISSN: 0027-8424
AU Waterhouse, Peter M.; **Graham, Michael W.**; Wang, Ming-Bo
AB Many examples of extreme virus resistance and posttranscriptional **gene silencing** of endogenous or reporter **genes** have been described in transgenic plants contg. sense or antisense transgenes. In these cases of either cosuppression or antisense suppression, there appears to be induction of a surveillance system within the plant that specifically degrades both the transgene and target RNAs. Transforming plants with virus or reporter **gene** constructs that produce RNAs capable of duplex formation confer virus immunity or **gene silencing** on the plants. This was accomplished by using transcripts from one sense **gene** and one antisense **gene** colocated in the plant genome, a single transcript that has self-complementarity, or sense and antisense transcripts from **genes** brought together by crossing. A model is presented that is consisted with these data and those of other workers, describing the processes of induction and execution of posttranscriptional **gene silencing**.

(FILE 'HOME' ENTERED AT 10:45:14 ON 12 NOV 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, EMBASE, BIOSIS, MEDICONF' ENTERED AT 10:45:23 ON 12 NOV 2002

L1 40392 S GENE (L) SILEN?
L2 3154 S L1 AND (TANDEM OR REPEAT)
L3 75 S L2 AND (SENSE OR ANTISENSSE)
L4 29 DUP REM L3 (46 DUPLICATES REMOVED)
L5 29 FOCUS L4 1-
L6 457 S D HIS
L7 9 S L5 AND PY<=1998

=> d an ti so au ab l7 2 3

L7 ANSWER 2 OF 9 AGRICOLA
AN 1999:22365 AGRICOLA
TI A transgene with repeated DNA causes high frequency, post-transcriptional suppression of ACC-oxidase gene expression in tomato.
SO The Plant journal : for cell and molecular biology, **Sept 1998.** Vol. 15, No. 6. p. 737-746
Publisher: Oxford : Blackwell Sciences Ltd.
ISSN: 0960-7412
AU Hamilton, A.J.; Brown, S.; Yuanhai, H.; Ishizuka, M.; Lowe, A.; Solis, A.G.A.; Grierson, D.
AB **Gene silencing** with **sense genes** is an important method for down-regulating the expression of endogenous plant **genes**, but the frequency of **silencing** is unpredictable. Fifteen per cent of tomato plants transformed with a 35S-ACC-oxidase (ACO1) **sense gene** had reduced ACC-oxidase activity. However, 96% of plants transformed with an ACC-oxidase **sense gene**, containing two additional upstream inverted copies of its 5' untranslated region, exhibited reduced ACC-oxidase activity compared to wild-type plants. In the three plants chosen for analysis, there were substantially reduced amounts of both endogenous and transgenic ACO RNA, indicating that this was an example of co-suppression. Ribonuclease protection assays using probes spanning intron-exon borders showed that the reduced accumulation of endogenous ACO mRNA occurred post-transcriptionally since the abundance of unprocessed transcripts was not affected. The ACO1 transgene with the repeated 5'UTR also strongly inhibited the accumulation of RNA from the related ACO2 **gene** in flowers, although there is little homology between the 5'UTRs of ACO1 and ACO2. These results indicate that although repeated DNA in a transgene greatly enhances the probability of **gene silencing** of an endogenous **gene**, it also involves generation of a trans-acting **silencing** signal produced, at least partly, from sequences external to the **repeat**.

L7 ANSWER 3 OF 9 AGRICOLA
AN 1998:28715 AGRICOLA
TI Post-transcriptional silencing of chalcone synthase in Petunia by inverted transgene **repeats**.
SO The Plant journal : for cell and molecular biology, **July 1997.** Vol. 12, No. 1. p. 63-82
Publisher: Oxford : Blackwell Sciences Ltd.
ISSN: 0960-7412
AU Stam, M.; Bruin, R. de.; Kenter, S.; Hoorn, R.A.L. van der.; Blockland, R. van.; Mol, J.N.M.; Kooter, J.M.
AB To induce post-transcriptional **silencing** of flower pigmentation **genes** by homologous **sense** transgenes in transgenic petunias, it is not necessary for the transgenes to be highly transcribed. Even promoterless transgenes can induce **silencing**. Here it is shown that in these cases **silencing** is mediated by multimeric transgene/T-DNA loci in which the T-DNAs are arranged as inverted **repeats** (IRs). With the transgene constructs used, monomeric T-DNA loci are unable to confer **silencing** even though they modulate IR-induced **silencing**. IRs with the **silencing** sequences proximal to the centre (IRc) induce a more severe **silencing** than IRs with these sequences distal to the centre (IRn). Somatic reversion of **silencing**, as observed in a side branch of one of the chalcone synthase (Chs) transformants, was associated with a deletion of the IR

locus from L1 cells, the meristematic cell layer that expresses the endogenous Chs **genes** in the flower corolla. Taken together, these data indicate that the post-transcriptional **silencing** mechanism can be activated by inverted transgene **repeats**. It is also shown that a **silent** IR UidA-ChsA locus **silences** the expression of a monomeric 35S promoter-driven UidA-ChsA transgene only in corollas where the endogenous Chs **genes** are highly transcribed. These results are consistent with a model in which an IR, by virtue of its palindromic sequence organization, is able to promote the production of aberrant RNAs from the endogenous homologs as a result of ectopic pairing.

L5 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2002:142846 CAPLUS
DN 136:178951
TI Improved methods of **gene silencing** in plant using inverted **repeat** sequences from NOS **gene**
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
IN Gutterson, Neal; Oeller, Paul
AB The present invention provides methods for inhibiting target **gene** expression, by expressing in a cell a nucleic acid construct comprising an inverted **repeat** and a **sense** or antisense region having substantial sequence identity to a target **gene**, wherein the inverted **repeat** is unrelated to the target **gene**. The inverted **repeat** is chosen from any suitable sequence and has the ability to form a double stranded RNA in the cell. N another preferred embodiment, the heterologous inverted **repeat** of the invention is from Agrobacteriumn tumefaciens NOS **gene** or from the 3' untranslated region of the NOS **gene**. In one embodiment, the improved **gene silencing** construct is expressed in a plant cell, where the transcript, or fragments thereof, is taken up by plant pathogens such as fungi, bacteria, nematodes, e.g., cyst and root knot nematodes, and insects, e.g., sucking insects, leading to **gene silencing** in the pathogen. In another embodiment, the improved **gene silencing** construct is expressed in a transgenic plant, and is used to regulate expression of the transgene. N another embodiment, the **gene silencing** vector is used to regulate expression of an endogenous plant **gene**, e.g., to regulate plant phenotypes such as disease resistance.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002014472	A2	20020221	WO 2001-US25538	20010814
WO 2002014472	A3	20020718		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001088257	A5	20020225	AU 2001-88257	20010814

L5 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:718761 CAPLUS
DN 134:203186
TI **Gene** expression: Total **silencing** by intron-spliced hairpin RNAs
SO Nature (London) (2000), 407(6802), 319-320
CODEN: NATUAS; ISSN: 0028-0836
AU Smith, Neil A.; Singh, Surinder P.; Wang, Ming-Bo; Stoutjesdijk, Peter A.; Green, Allan G.; Waterhouse, Peter M.
AB Post-transcriptional **gene silencing** (PTGS), a sequence-specific RNA degrdn. mechanism inherent in many life forms, can be induced in plants by transforming them with either antisense or co-suppression constructs, but typically this results in only a small proportion of **silenced** individuals. Here we show that **gene** constructs encoding intron-spliced RNA with a hairpin structure can induce PTGS with almost 100% efficiency when directed against viruses or endogenous **genes**. Using principles we developed for **silencing** constructs that express double-stranded RNA and inverted-**repeat** RNA, we made a construct encoding a single self complementary hairpin RNA (hpRNA) of the Niaprotease (Pro) **gene** sequence of potato virus Y (PVY). The construct contains **sense** and antisense Pro sequences flanking a nucleotide spacer fragment derived from uidaA (GUS) **gene**. About 60% of the plants that are transformed with the constructs were immune to the virus. In the next expt., we replaced the spacer with an intron sequence, which is spliced out during pre-mRNA processing to produce loopless hpRNA. As a

control, the intron sequence was inserted in the reverse, non-splicing, orientation. When transformed into tobacco, 22 of 34 (65%) reverse-intron plants were immune, a similar frequency to plants transformed with the GUS spacer construct. Amazingly, 22 of 23 plants transformed with the construct contg. the functional intron were immune to the virus. This same enhancement was obsd. when hpRNA constructs against the endogenous .apprch.12-desaturase (Fad2) **gene** of Arabidopsis, in which 100% (30/30) of plants transformed with the intron construct showed **silencing** of the **gene**. The process of intron excision from the construct by spliceosome might help to align the complementary arms to the hairpin in an environment favoring RNA hybridization, promoting the formation of a duplex. Alternatively, splicing may transiently increase the amt. of hairpin RNA by facilitating, or retarding, the hairpin's passage from the nucleus, or by creating a smaller, less nuclease-sensitive loop.

L5 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2001:507844 CAPLUS
DN 135:88019
TI Compositions and methods for **gene silencing** by expression of double-stranded RNA
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
IN Driscoll, Monica; Tavernarakis, Nektarios
AB DNA constructs are provided for disrupting gene expression in targeted organisms, including humans, mice, plants, insects, and nematodes. The DNA constructs involve a transcription promoter followed by a gene coding sequence in the **sense** orientation linked to the same coding sequence in an antisense orientation followed by a transcription terminator. Use of a DNA construct, which is an inverted **repeat** (IR) of a gene cloned in an expression vector, for treatment of Alzheimer's and Parkinson's disease and tomato leaf curl virus is claimed. RNA interference by double-stranded RNA using methods claimed in this invention was demonstrated in Caenorhabditis elegans and was more effective compared to gene disruption methods such as injection of dsRNA and expression of an antisense DNA strand alone. For some but not all genes tested, transgenic C. elegans lines contg. extrachromosomal IR gene constructs under control of the heat shock-inducible promoter hsp16-2 had high percentages of progeny with the predicted phenotype for deletions of the gene used in the construct. C. elegans gene C37A2.5 required for development past the L2 larval stage, gene F26F12.7 required for fertility, and gene mec-4 required for touch sensitivity could be disrupted by the claimed methods while genes efk-1 and unc-119 were not affected. The ability of an hsp16-2 promoter-green fluorescent protein (GFP) gene IR construct to affect expression of an integrated GFP gene in C. elegans was also demonstrated.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001049844	A1	20010712	WO 2001-US126	20010102

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

L5 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2002:575187 CAPLUS
DN 137:122370
TI **Sense** and antisense constructs for silencing of barley yellow dwarf virus-PAV RNA dependant RNA polymerase and improved viral resistance of cereal plants
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
IN Waterhouse, Peter; Wang, Ming-Bo; Abbott, David
AB The invention provides a DNA mol. comprising a plant-operable promoter operably linked to a DNA region that is capable of being transcribed in

the cells of a cereal plant to produce RNA comprising inverted **repeat** sequence least about 19 nucleotides from the sequence of an RNA dependent RNA polymerase **gene** of Barley Yellow Dwarf Virus (BYDV). These constructs encode **sense** and antisense RNA mols. and are directed to the RNA dependent RNA polymerase **gene**. The RNA is capable of forming an artificial hairpin RNA structure with a double stranded RNA stem by base-pairing between the regions with **sense** and antisense nucleotide sequence such that at least the 19 consecutive nucleotides of the **sense** sequence base pair with the 19 consecutive nucleotides of the antisense sequence resulting in an artificial hairpin structure. The DNA mol. is useful for reducing expression of the viral RNA dependant RNA polymerase and for enhancing the resistance of cereal crops to BYDV, optionally in the presence of a viral product that normally inactivates other modes of post transcriptional **gene silencing**. Methods are provided for producing transgenic cereal plant lines comprising the DNA mol. of the invention integrated into their genome, and selecting those lines having resistance to BYDV infection. Transgenic plants having enhanced resistance to BYDV are also provided.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002059257	A2	20020801	WO 2001-IB2737	20011031

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

L5 ANSWER 5 OF 29 MEDLINE

AN 2001418932 MEDLINE

TI Double-stranded RNA-mediated silencing of genomic **tandem repeats** and transposable elements in the D. melanogaster germline.

SO CURRENT BIOLOGY, (2001 Jul 10) 11 (13) 1017-27.
Journal code: 9107782. ISSN: 0960-9822.

AU Aravin A A; Naumova N M; Tulin A V; Vagin V V; Rozovsky Y M; Gvozdev V A

AB BACKGROUND: The injection of double-stranded RNA (dsRNA) has been shown to induce a potent sequence-specific inhibition of **gene** function in diverse invertebrate and vertebrate species. The homology-dependent posttranscriptional **gene silencing** (PTGS) caused by the introduction of transgenes in plants may be mediated by dsRNA. The analysis of Caenorhabditis elegans mutants impaired with dsRNA-mediated **silencing** and studies in plants implicate a biological role of dsRNA-mediated **silencing** as a transposon-repression and antiviral mechanism. RESULTS: We investigated the **silencing** of testis-expressed Stellate **genes** by paralogous Su(Ste) **tandem repeats**, which are known to be involved in the maintenance of male fertility in Drosophila melanogaster. We found that both strands of repressor Su(Ste) **repeats** are transcribed, producing **sense** and antisense RNA. The Stellate **silencing** is associated with the presence of short Su(Ste) RNAs. Cotransfection experiments revealed that Su(Ste) dsRNA can target and eliminate Stellate transcripts in Drosophila cell culture. The short fragment of Stellate **gene** that is homologous to Su(Ste) was shown to be sufficient to confer Su(Ste)-dependent **silencing** of a reporter construct in testes. We demonstrated that Su(Ste) dsRNA-mediated **silencing** affects not only Stellate expression but also the level of **sense** Su(Ste) RNA providing a negative autogenous regulation of Su(Ste) expression. Mutation in the spindle-E **gene** relieving Stellate **silencing** also leads to a derepression of the other genomic **tandem repeats** and retrotransposons in the germline. CONCLUSIONS: Homology-dependent **gene silencing** was shown to be used to inhibit Stellate **gene** expression in the D. melanogaster germline, ensuring male fertility. dsRNA-mediated **silencing** may provide a basis for negative autogenous control of **gene** expression. The related surveillance system is implicated to control expression of